

## CLAIMS

What is claimed is:

1. A method of modulating cell death in a eukaryotic cell, comprising contacting the cell with an agent that modulates a biological activity of DNA-PK.
2. The method of claim 1, wherein the biological activity of DNA-PK is a kinase activity of DNA-PKcs.
3. The method according to claim 2, wherein DNA-PKcs kinase activity is increased in the cell, thereby decreasing cell death.
4. The method according to claim 1, wherein the agent comprises an immunomodulatory nucleic acid molecule.
5. The method according to claim 2, wherein DNA-PKcs kinase activity is decreased in the cell, thereby increasing cell death.
6. A method of reducing cell damage mediated by a hypoxic condition, comprising contacting the cell with an agent that modulates a biological activity of DNA-PK.
7. The method of claim 6, wherein said agent is an immunomodulatory nucleic acid molecule.
8. A method for identifying an agent that modulates a biological activity of DNA-PK, comprising:

a) adding an agent to be tested to a sample, the sample comprising DNA-PK and an immunomodulatory nucleic acid molecule, under conditions which favor binding of the immunomodulatory nucleic acid molecule to DNA-PK, thereby forming a test sample; and

b) detecting a biological activity of DNA-PK protein in the test sample, as compared to a control sample lacking the agent, wherein an increase or a decrease in the biological activity of DNA-PK indicates that the agent modulates a biological activity of DNA-PK.

9. The method of claim 8, wherein the biological activity of DNA-PK is binding to an immunomodulatory nucleic acid molecule.

10. The method according to claim 9, wherein the method is a cell-free method, and the immunomodulatory nucleic acid molecule is detectably labeled.

11. The method of claim 8, wherein the biological activity of DNA-PK is activation of DNA-PKs kinase activity.

12. The method of claim 8, wherein the method is a cell-based method and modulation of DNA-PK activity is detected by measuring an amount of IL-6 or IL-12 produced by the cell.

13. A composition comprising:

- a) an agent identified by the method of claim 8; and
- b) a pharmaceutically acceptable excipient.

14. A method for reducing DNA damage in a eukaryotic cell, comprising contacting the cell with an agent that modulates a biological activity of DNA-PK.

15. The method of claim 14, wherein the biological activity of DNA-PK is a kinase activity of DNA-PKcs.

16. The method of claim 15, wherein said agent is an immunomodulatory nucleic acid molecule.

17. A method of reducing cell death in an individual, comprising administering to an individual an effective amount of an agent that modulates a biological activity of DNA-PK.

18. The method of claim 17, wherein the cell death is triggered by an ischemic condition.

19. A method of reducing cell death in an organ, comprising contacting a cell of the organ with an effective amount of an agent that modulates a biological activity of DNA-PK.

20. The method of claim 19, wherein the contacting is performed *ex vivo*.